THE SEQUENCE OF THE PATHOLOGICAL CHANGES IN ACUTE APPENDICITIS AND APPENDICULAR PERITONITIS.

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The study upon which this paper is based was originally undertaken with the idea of tracing the progress of the processes of inflammation and repair in cases of acute appendicitis both as regards the primary appendicular inflammation and the complicating peritonitis. During the course of the study I have examined microscopically 539 appendices removed during or within ten days following an acute attack, and I have studied the gross pathology as found at operation in more than fifteen hundred cases of appendicitis. In every instance the pathological data has been classified especially with reference to the duration of the symptoms previous to the time of the observation of the pathological conditions. As regards the appendicitis itself, the time was figured from the first onset of symptoms while as regards the more extensive peritoneal involvements it was found necessary to determine not only the time of the beginning of the attack but also approximately the time of occurrance of any exacerbations of peritoneal symptoms.

When the lesions are studied in this way in a sufficiently large series of cases the progress of the processes of inflammation and repair can be readily traced. Furthermore, it is apparent that most of the so-called varieties of acute appendicitis represent only different stages of development of the inflammatory process, and in spite of minor variations in the intensity and extent of the destructive process there is found to exist a striking general similarity in the fundamental pathological changes as they occur at each of the succeeding periods following the onset of symptoms.[1] In fact, if we stop viewing the appendices removed at operation as museum curiosities and study them as examples of a disease process, grouping them according to the day of the disease in which they are removed, it is surprising how fundamentally alike are the specimens removed during each succeeding day of the attack.

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[1] We frequently hear statements to the effect that in appendicitis it is often impossible to predict with any degree of accuracy from the clinical symptoms the pathology existing in the abdomen. This is true as regards diagnoses based on the physical findings alone, but it should not be true as regards diagnoses based on the physical findings plus a good working knowledge of the pathology of each day of the disease. Given the date of the onset of attack, the time of any acute exacerbation of peritoneal symptoms, if such there has been, and the physicial findings as regards the extent of abdominal rigidity, and one should be able to predict the pathology with an accuracy not surpassed in any other intra-abdominal condition with which I am familiar.

Even more uniform is the sequence of changes in the complicating peritonitis, for if peritonitis be studied as a disease process it will be found that as regards any given area of involvement the lesions, of say eighteen hours' duration, present certain fundamental features which are essentially similar in each case. Likewise forty-eight hour cases present features typically characteristic of the forty-eight hour stage of the infection, and so on from day to day throughout the course of the disease.[2]

In this paper I shall not attempt to detail the occasional, and for practical purposes unimportant, variations from the usual progress of the disease. Those interested in this phase of the subject I would refer to Aschoff's monograph[3] on the pathology of appendicitis and to my paper published in 1905.[4]

It is interesting to note, however, that in the later cases studied by me the variations from the average have been much less noticeable than in the earlier cases, probably in part because of more accurate histories, but very largely because in most of the later cases the appendix and surrounding organs had been kept at rest by therapeutic means during the time between the onset of symptoms and the operation.

First Day. The pathological changes found during the first twenty-four hours of an attack of appendicitis are essentially similar in nearly all cases. I have never seen a real case of acute appendicitis operated at this stage of the disease in which a definite obstruction of the lumen of the appendix was not demonstrable. Proximal to this point of obstruction the appendices show little, if any, noteworthy pathological changes. Distal to the point of obstruction, the appendices are constantly distended to a point approximating the maximum distensibility of the organ. After the first eight or ten hours of the attack, fibrin is usually found on the peritoneal surface, and toward the close of the first twenty-four hours a considerable proportion of the appendices show macroscopic evidences of beginning gangrene. The true gross pathology of the first day of appendicitis can only be observed at the operating table because the loosening of peritoneal tissue bands incident to removal of the appendix, removes the causal obstruction or, if the obstruction is due to impacted fecolithes, these are often displaced during the manipulations so that by the time the appendix reaches the laboratory the complete picture of the gross pathology is usually lost.

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[2] This statement as regards the changes occurring in any given area of involved peritoneum is based not alone on the observations made in cases of appendicular peritonitis, but has been checked by observations made at operation and postmortem in peritonitis of widely different origins such as perforating gastric ulcer and ruptured pyosalpinx. The question as to the frequency with which these lesions under favorable conditions will progress to resolution or local abscess formation must be determined from actual experience. That it is the rule in cases of pelvic peritonitis is well known to all, but there is as yet a difference of opinion as to how frequently it actually does occur in unoperated cases of appendicular peritonitis.

[3] Die Wurmfortsatzentzundung, Jena, 1908.

[4] Stanton, E. MacD., The Sequence of Pathological Changes in Appendicitis, Jour. Amer. Med. Assoc., June 10, 1905.

The microscopic changes of the first day consist of an intense diffuse, polynuclear leukocytic infiltration with in all but the milder cases, focal areas of hemorrhages and necrosis involving all coats with a more or less extensive destruction of mucosa, and in many cases a fibrinous or fibrino-purulent exudate on the peritoneal surface. One of the most striking features in these early cases is the presence throughout the majority of the sections of numerous focal areas of necrosis. These areas are larger but are not as a rule more numerous in those cases which show macroscopic evidences of gangrene.

Many writers on the pathology of appendicitis would have us believe that acute appendicitis begins as a catarrhal inflammation of the mucosa, extending to the lymphoid tissue of the submucosa and finally through the muscular coats to the peritoneum, thus inferring that so-called catarrhal appendicitis is an early stage of the acute process. In ten years' time, in which I have made a microscopic examination of practically every first-day appendix that I could lay my hands on, I have never found a single instance of catarrhal appendicitis in a specimen removed during the acute stage of the attack. The diffuse infiltration of all coats is demonstrable even in cases operated within five or six hours of the onset of the first symptoms. Moreover, I have never seen an example of so-called catarrhal appendicitis diagnosed as such by other pathologists which, on referring back to the clinical history, did not prove to be either an appendix removed at an interval operation or a symptomless appendix removed incidental to other intra-abdominal surgery.[5] I believe this question of catarrhal appendicitis is worthy of emphasis for I am certain that the acceptance on the part of general practitioners and surgeons of the belief that catarrhal appendicitis is really a clinically important pathological entity has led to many grave errors in the field of appendiceal surgery.

The peritoneal lesion of this first day is essentially a fibrinous or serofibrinous exudate. On the surface of and in the immediate neighborhood of the appendix the primary exudate seems always to be of a dry, fibrinous character. In the cases studied by me extensive serous exudates have been found only toward the close of the first twenty-four hours of the attack, and then only in cases which had been given strong cathartics soon after the onset of the symptoms.

Even in the presence of a fluid exudate of greater or less extent at this stage of the disease the general peritoneum is smooth, and aside from a more or less intense congestion of the subendothelial bloodvessels there is little evidence of a true peritonitis.

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[5] Kocher (Cor. Bl. f. Schweize Aerzte Basel, 1913, xliii, 1633) in a recent discussion of this subject says, "I see appendicitis catarrhalis only as a chronic form and as a residue after earlier acute attacks."

From a surgical view-point I believe that the peritoneal involvement of the first day may in nearly all cases be ignored and the abdomen closed without drainage. This assertion is, I am certain, borne out by clinical experience, and bacteriological studies (Kelly,[6] Watzold,[7] Cohn,[8] Aschoff,[9] DeQuervain[10]) show that in the majority of cases this first-day exudate is free from bacteria.

I have dealt somewhat at length on the first day's pathology in acute appendicitis because it is the foundation upon which the subsequent course of the disease is based.[11]

Second Day. Beginning with the second day of the attack, the peritoneal involvement, which is present to a greater or less extent in over half of the cases, assumes great practical importance and from now on we are really dealing in the majority of cases with two pathological conditions which must be described separately. First the inflammed appendix, and second the associated peritoneal infection.

In the appendix itself we find a continuation of the inflammatory process begun on the first day. Owing to a coalescence of the microscopic areas of necrosis seen in the first day cases there is by the second day a decided increase in the frequency of macroscopic areas of gangrene. Gross perforation of the appendix itself, with or without gangrene, if it is going to occur at all usually takes place before the end of the second day.[12]

Microscopically, second-day appendices show an intense leukocytic infiltration involving all coats together with a more or less extensive ulceration of the mucosa, while over 70 per cent. show

[6] The Vermiform Appendix, 1905.

[7] Quoted by Aschoff.

[8] Arch. f. klin. Chir., Bd. 85, Heft 3.

[9] Loc. cit.

[10] Cor.-Bl. f. Schweize Aerzte, 1913, xliii.

[11] I believe that the pathology of this first day corresponds closely with the clinical symptoms. First, we have the obstruction causing the primary colic which, like all other colics originating in the gastro-intestinal tract, is, as a rule, referred by the patient to the pit of the stomach or mid-abdominal region. As in gall-stones, strangulated hernia and other obstructive lesions in the gastro-intestinal tract this colic is usually accompanied by nausea and vomiting. It is interesting to note that pressure over the appendix at this very early stage often causes an increase in the pain referred to the umbilical region. A few hours later, with the development of the inflammatory reaction in the appendix, we have a new subjective pain due to the inflammation itself and referred by the patient to the region of the appendix. Local tenderness and rigidity apparently develop with the first involvement of the peritoneal covering of the appendix.

[12] The term perforation as applied clinically and meaning a sudden increase in peritoneal involvement has, I believe, little definite relationship to gross perforations of the appendix itself but rather to the sudden giving away of adhesions limiting a peri-appendicular infection. Histological studies would seem to show that the great majority of appendices are bacteriologically perforated early in the attack, and that protection of the general peritoneal cavity against the infection depends far more upon the maintainance of the integrity of the fibrinous protecting adhesions surrounding the appendix than upon the bacterial impermeability of the inflammed wall of the appendix itself.

a well-marked fibrinopurulent exudate on the peritoneal surface. In those cases which presented macroscopic evidences of gangrene the areas of necrosis as seen microscopically are decidedly more extensive than in the similar cases of the first day group, while in those cases which did not present microscopic evidences of gangrene the focal areas of necrosis, so prominent in the first day cases, are still evident in the majority of sections, but are often obscured by the leukocytic infiltration.

THIRD DAY. By the third day the destructive process in the appendix itself has, in the majority of cases, reached its maximum both as regards the macroscopic and microscopic evidences of disease.

Histologically, the third-day appendices show a diffuse inflammation of the same character as that seen in earlier groups. In the macroscopically gangrenous cases the necrosis is prominent, while in the non-gangrenous cases focal areas of necrosis are seen only in the mucosa. The most striking histological feature which distinguishes this group from the earlier groups is the evidence of beginning repair as seen by the presence of fibroblasts in all sections. These new-formed connective-tissue cells are especially numerous in the region of the peritoneum, although present in other areas, particularly in those cases showing the least marked leukocytic infiltration.

From the third day on changes in the appendix itself have chiefly to do with the process of repair which proceeds with surprising rapidity, the histological picture varying from day to day in the same manner as in any other inflammatory process undergoing repair by organization. However, the rapidity of the repair varies considerably in different cases, being slowest in those cases accompanied by extensive gangrene and most rapid in those cases accompanied by the least primary destruction.

FOURTH DAY. The fourth day is characterized chiefly by an increase in the evidences of repair. Microscopically the gangrenous cases show large areas of complete necrosis, the histologic picture differing but little from that seen in the gangrenous cases of the third-day group. In sections of the non-gangrenous cases and in sections taken at some distance from the necrotic areas in the gangrenous appendices, the most noticable histologic feature which distinguishes this group from the preceding one is a decided increase in the relative number of fibroblasts and the presence of numerous lymphocytes, and in many cases plasma cells. In those cases accompanied by a peri-appendicular exudate a few fibroblasts and many new-formed bloodvessels can be seen extending into the exudate from the peritoneal surface. Focal areas of hemorrhage into the exudate occurring from these new-formed bloodvessels and frequently seen in the sections.

FIFTH DAY. The microscopic lesions of the fifth day may be classified into two rather sharply defined groups. In the cases presenting macroscopic evidences of gangrene, the necrosis and polynuclear leukocytic infiltration is still the predominating characteristic, although the repair process is well advanced in some instances. In the non-gangrenous cases the polynuclear leukocytes have practically disappeared except at the surfaces of the ulcerations in the mucosa and of the peri-appendicular exudates. Throughout the coats of the appendix there is a marked increase in the number of fibroblasts and often an intense lymphocytic infiltration. In the peri-appendicular exudates the new-formed bloodvessels penetrate to a greater distance than in the fourth-day group, and this granulation tissue is decidedly richer in fibroblasts.

SIXTH AND SEVENTH DAYS. Histologically, the repair processes are seen on the sixth and seventh days are decidedly more advanced than in the fifth-day group. The gangrenous cases show well-marked evidences of repair, the histological picture of which is similar to that seen in the non-gangrenous cases of the preceding group. The non-gangrenous cases now show areas in which the fibroblasts are massed together and elongated so as to resemble young connective tissue cells. Small ulcers in the mucosa have apparently been largely repaired.

SECOND WEEK. After the first six or seven days the repair processes in all but the most extensively damaged organs are so far advanced as to present microscopic pictures of a subacute or chronic character. Even in the more severely damaged appendices the repair proceeds rapidly, and as a rule results ultimately in a surprisingly complete restitution of the organ.

Acute recurrences following dietary or other causes if they occur at this stage result in the engrafting of a new acute lesion upon the histological picture of partial repair. Evidences of this type of acute recurrence were rather common in my earlier cases, but while I suspect the too free use of cathartics and dietary errors as the cause I have not been able to collect any really trustworthy evidence on this point. The fact remains, however, that in more recent years I have not observed more than three or four appendices showing an acute lesion engrafted upon a subacute process.

APPENDICULAR PERITONITIS. Before describing the progress of the pathological changes associated with the complicating peritoneal infection I would emphasize the fact that the distribution of this infection in the peritoneal cavity seems to be dependent very largely upon purely mechanical factors.

It is a popular assumption that the extent and seriousness of the peritoneal infection bears a rather definite relation to the extent of the destructive lesion in the appendix itself, but fluid exudates frequently occur without gangrene or actual perforation, and cases are frequently observed with extensive gangrene which must have existed for several days without the presence of peri-appendicular pus, showing that other factors, such as the resistance of the patient, peristalic movements, and the virulence of the infecting organisms must play an important part in determining the character of the lesion during the early stages of the inflammation. Instead of finding gangrenous and perforated appendices associated with an extensive and severe peri-appendicular peritonitis it is the rule to find very limited peritoneal involvement, in spite of the most estensive destructive lesions of the appendix itself, in all of those cases referred by physicians who have from the first directed their treatment toward the prevention of the mechanical spread of the infection.

Surgeons may honestly differ as to the advisability of immediate operation in certain stages of the disease, but there can be no question as to the advisability of treating every case of even suspected appendicitis by the so-called Ochsner treatment until the diagnosis is possible, and the services of the surgeon procured.

In this connection I cannot do better than quote from Mr. Moynihan,[13] of Leeds, who says: "It is now about seven years since I was first brought firmly to the conviction that in cases of appendicitis it is the administration of an aperient that is responsible for the acute castastrophe of gangrene and perforation which ends in an acute peritonitis. I do not remember one single case that I have operated upon since in which it was not perfectly clear that the same sequence of events—pain, aperient, perforation—had occurred, and I therefore do not hesitate to say that in almost every instance of acute peritonitis due to the perforation of an appendix it is the treatment directed to the relief of the condition that is the cause of the serious and so often fatal catastrophe. The taking of a purgative medicine is something more than an impressive antecedent —it is, in my judgment, a definite cause. The only possible exceptions occur in those rare cases where direct violence gives rise to a rupture of the appendix or the laceration of the adhesions which enwrap it. In cases of appendicitis, however acute their origin may be, perforation followed by an acute general peritonitis does not seem to occur if no aperient is given and if absolute starvation is adopted from the first. The acute spreading or general peritonitis which occurs in this disease is due to treatment; it is a 'therapeutic peritonitis.' I am quite prepared to learn that this emphatic statement is received with a shrug of doubt and the tolerant smile of disbelief, but if strict inquiry is made into the intimate details of the history of the cases I cannot think that my experience of this disease will prove to be singular. In appendicitis, *perforation spells purgation.*"

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[13] Acute Emergencies of Abdominal Disease, British Med. Jour., April 1, 1911.

Deaver[14] emphasizes this same point as follows: "Perhaps the most important question that concerns the internist and practitioner, as well as the surgeon, is the use of purgatives during the acute stage of the disease. It is not long since we all thought that a purge should be administered in the initial stages of the disease, but we have come to realize that the contents of the bowel play practically no part in the continuation of the disease, while the peristalsis induced by purgation has proved to be a most unfavorable factor, defeating the end and principle upon which our treatment is based—namely, anatomical and physiological rest. The purgative is more deadly than the scalpel. Of this I have long been convinced, but with a view to obtaining exact figures to support my contention, I have had the year's work analyzed with respect to this point. Among 259 adults there were 79 that had a history of being purged before admission. Of these 79 cases all save 2, at the time of operation, showed appendices that were either perforated, gangrenous, acutely ulcerated, or surrounded by an abscess. The remaining 2 only were simple catarrhal inflammation. Of the 7 deaths occurring in the series 5 were purged before admission. Of those drastically purged, 97.5 per cent. showed the severest kinds of appendicular disease. The exact figures are here given:

"Pathological lesion of appendix: perforation, 30; gangrene, 9; acute ulcerative and suppurative, 23; peri-appendicular abscess, 15; acute catarrhal, 2.

"Among 100 children the same rule holds. There were 56 that had been vigorously purged. Of these, 86 per cent. showed the more serious lesions, such as gangrene, perforation, abscess, etc. Twelve cases had diffuse peritonitis, all of which had been purged before admission. The table is as follows:

"Pathological lesion: perforation, 22; gangrene, 15; acute ulcerative, 6; peri-appendicular abscess, 4; acute catarrhal, 8; indefinite, 1.

"In this series there were 44 acute cases that were not purged, and in this group there was but one case of perforation, 8 cases of gangrene, and no peri-appendicular abscesses."

My own conception based on pathological and clinical studies is that the great majority of appendices are bacteriologically perforated after the first few hours of the attack irrespective of whether or not there is a gross perforation or gangrene evident to the naked eye, and that the protection of the general peritoneal cavity from infection depends upon the maintainance of the integrity of the fibrinous peri-appendicular protecting adhesions rather than upon the bacterial impermeability of the wall of the appendix itself.

As stated above the peritoneal lesion of the first day of the attack is essentially a fibrinous or serofibrinous exudate. On the surface of and in the immediate neighborhood of the appendix the primary exudate seems always to be essentially of a dry, fibrinous character. In cases studied by me extensive serous or seropurulent exudates have been found only toward the close of the first twenty-four hours of the attack, and then only in cases which had been given strong cathartics soon after the onset symptoms.

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[14] A Year's Work in Appendicitis, Trans. Coll. of Phys. of Philadelphia, 1912, xxxiv, 227.

The peritoneal lesions encountered after the first day of an attack of appendicitis may be divided into two sharply defined groups: (1) those cases in which the inflammed appendix is protected from the general peritoneal cavity by a zone of fibrinous exudate massing together continguous intraperitoneal structures, usually the omentum, the head of the cecum, a portion of the parietal peritoneum, and one or two loops of small intestines, with or without a localized collection of pus in the immediate vicinity of the appendix, and (2) cases with more or less diffuse peritoneal involvement. It is this latter class of cases which gives to appendicitis its mortality, and it is of the greatest practical importance for us to have a clear conception of the sequence of the pathological changes as they occur in this complication of appendicitis.

The time of onset of the more diffuse peritoneal involvement can nearly always be determined from the clinical history. Usually the onset of well marked peritoneal symptoms follows a few hours after the giving of a cathartic on the first or second day of the disease, although, we not infrequently find that the acute exacerbation of peritoneal symptoms occurs on the third or some subsequent day—a so-called late perforation. Such acute exacerbations are almost invariably the result of giving food or cathartics by mouth or of active muscular movements on the part of the patient. At operation these cases of late "perforation" show peritoneal lesions of different ages, almost invariably a lesion of limited extent in the region of the appendix with a pathological picture corresponding to the day of the disease and a more or less diffuse lesion with a pathology dating from the time of the acute exacerbation.

Cases operated during the first twenty-four hours following a so-called perforation show that the first exudate thrown out by the peritoneum under these conditions is essentially a fluid exudate, and at first of a distinctly serous or sero-purulent character.[15] The

[15] A. V. and E. Moschcowitz (Arch. f. klin. Chir., 1907, Bd. lxxxii. 707), in reporting the pathological findings in 313 cases of appendicitis accompanied by peritonitis, deny that they found any evidence that serous, seropurulent and purulent peritonitis represent different stages of the same process because figuring from onset of the attack of appendicitis there was only a slight difference in the time at which these three forms of peritonitis were encountered at operation. They believe that it is far more probable that the three forms represent differences in the virulence of the infection, and differences in reaction on the part of individual patients. Similar observations were made by me in my earlier studies when my data was limited to that found in hospital histories but this apparent contradiction to the usual phenomena of inflammation promptly disappeared when I began to study cases coming under my personal observation, and was able to determine not only the time of the onset of the primary appendicitis but approximately the time of onset of the complicating peritonitis.

peritoneal surfaces during the first few hours are still smooth, and aside from a moderate congestion of the subendothelial vessels, there is little change in the peritoneum itself. In fact, except for the extent of the distribution of the fluid exudate, it is usually difficult to say just how far the peritonitis really does extend.

Following the first outpouring of serum, which gives to the first day its predominating characteristic, we have a continued migration of leukocytes and production of fibrin so that by the second day the intraperitoneal exudate, which is usually of considerable extent, is found to be distinctly seropurulent or purulent in character. The peritoneal surfaces now show more or less loss of lustre with here and there adherent flakes of fibrin, but they do not as yet show the marked roughening seen after the beginning of organization on the third day, and the absence of well-defined limiting adhesions is still a noticeable feature of the pathology.

It is during this second day of the peritoneal involvement that the serous surfaces continue to lose their lustre and that the relatively harmless exudate of the first day changes to the distinctly purulent exudate so characteristic of the third day and later cases. Likewise it is at this period that the mortality in operative cases begins to rise very rapidly.

It is well to note here that Murphy[16] in his reports of so-called diffuse peritonitis deals entirely with peritoneal lesions of under forty-eight hours' duration. As far as I know, Murphy does not report a single case of over forty hours' duration, and in a discussion before the Chicago Medical Society he referred to the third and fourth day lesions as cases of "pocketed" peritonitis which corresponds to my own observations concerning the sequence of changes in peritonitis. In other words, we must remember that the "diffuse" lesion described by Murphy by the onward march of the pathological process ends about the close of the second day of a peritoneal infection.

By the third day the continued fibrin production, together with the leukocytic migration, has resulted in transforming our previously diffuse fluid exudate into irregularly pocketed collections of pus. Limiting adhesions are now fairly well developed in most instances, but the lesions are as yet of a decidedly diffuse character, the area involved being much more extensive than at a later period, and there is as yet little or no evidence of the formation of sharply defined abscess cavities. The gross changes in the involved peritoneum, especially in the immediate neighborhood of the appendix, are now very noticeable, due in part to the more abundant fibrin, but chiefly to the changes in the peritoneum incident to the beginning organization which seems in all cases first to become noticeable on the third day following the involvement of any given area of peritoneum.

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[16] Perforative Peritonitis, Surg., Gyn., and Obst., June, 1908.

I believe that the subsequent course of the disease depends largely on whether or not the inflamed peritoneal surfaces are allowed to remain in the same relative position one to another. Certain it is if at this stage, or earlier, we put our peritoneum at rest by withholding food and cathartics and administering opiates in suitable quantities, we find that by the fourth or fifth day all fibrinous adhesions are being replaced by organizing granulation tissue which is also noticeable over the surfaces of the peritoneum in direct contact with the purulent fluid exudate. This granulation tissue serves not only to limit but to encapsulate the pus, and it is from this time on that the formation of definitely defined abscess cavities is observed. These abscesses are at first usually more or less multilocular but later become more localized to form, usually one well-defined cavity. The first evidences of the formation of a true abscess cavity are observed on the fifth or sixth day following the onset of the infection, although it is not until the seventh or eight day that the cavities become sharply defined with limiting adhesions firm enough to permit such manipulations as the packing away of the non-involved intestines without great danger of accidentally opening the abscess at some undesired point.

After the process of organization is well established on the fourth or fifth day there is every evidence of a progressive diminution in the extent of the peritoneal involvement which becomes less extensive as the abscess cavity becomes more sharply localized by the organizing adhesions.

This phase of the repair process which results in the more or less complete resolution of the peritoneal lesion beyond the immediate wall of the abscess has been well shown in a number of cases coming to operation on the tenth and eleventh days, the clinical picture in each having been on admission that of a severe diffuse peritonitis. In these cases the abscess cavities were surrounded by a narrow zone of organizing adhesions, while the peritoneum of the ascending colon and nearby loops of small intestines beyond the wall of the abscess cavity, although non-adherent, was thickened, reddish, and distinctly granular without fibrin or other evidences of an acute lesion. The clinical picture was on the third and fourth days undoubtedly that of a diffuse peritonitis, and this view is confirmed by the pathological findings as observed later at operation, although by the tenth or eleventh day the diffuse lesion had so far cleared up as to leave but slight, though unmistakable, evidences of its having existed.

SUMMARY AND CONCLUSIONS. In conclusion I would emphasize the following points:

1. Acute appendicitis is even during the first day of the attack a diffuse inflammatory process involving all coats of the appendix.

2. The destructive process in the appendix reaches its height on the second and third days of the disease. From the third day

on the subsequent changes occurring in the appendix itself have chiefly to do with the repair of the damage done during the earlier periods of the attack.

3. The diffuse inflammatory process involving the walls of the appendix is of such character that even without gross evidences of perforation the protection of the general peritoneal cavity from infection depends upon the maintainance of the integrity of the fibrinous periappendicular adhesions rather than upon the bacterial impermeability of the walls of the appendix itself.

4. My observations lead me to agree with Deaver, Moynihan, Ochsner and others when they state that clinical perforation would almost never occur if the general practitioner and the laity would appreciate the fact that in appendicitis "perforation spells purgation" and withhold cathartics during the early stages of suspected cases.

5. If in cases of diffuse peritonitis the peritoneal surfaces are put at rest by withholding food and cathartics by mouth the sequence of subsequent changes occurring in the involved area represents a definite and essentially uniform process tending to the resolution of the lesion or the formation of definitely circumscribed abscesses.

6. After the first thirty-six to forty-eight hours of a diffuse peritoneal infection the lesions encountered are of such a character as to be essentially undrainable and not well suited to surgical interference, a condition which continues until the period of localized abscess formation.

TUBERCULOSIS OF THE VULVA.

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Since Koch,[59] in 1882, published his paper, there has grown up an enormous literature on the subject of tuberculosis. Among this can be found in nearly every language excellent and complete descriptions of the disease in its various forms. But although the process in the more common locations has been frequently described, some of the rarer manifestations have received but meager attention. It is the object of this paper to report a new case of tuberculosis of the vulva and to collate the scattered literature on the subject.

The following case has recently come under my observation. Mrs. G. M., aged forty-one years, was first seen in October, 1913. Her history at that time was as follows: Married, husband suffering from pulmonary tuberculosis, but as far as could be ascertained